The Need for Harmonization in Biobanking to Realize the Potential of 21st Century Medicine

IBM World Wide Biobank Summit IV

November 8, 2005

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Outline

- Vision for the Future: Molecular Oncology/Medicine
- Conquering Cancer: Why is cancer so “hard” and why are biospecimens so critical? – Why do we need change now?
- NCI’s Approach to Biospecimens and Biorepositories
- Actions and Reactions
- The Future – NCI and Global Harmonization

Molecular Oncology: The Convergence of Molecular Biology/Genetics, Advanced Technologies, Bioinformatics, and Broadband

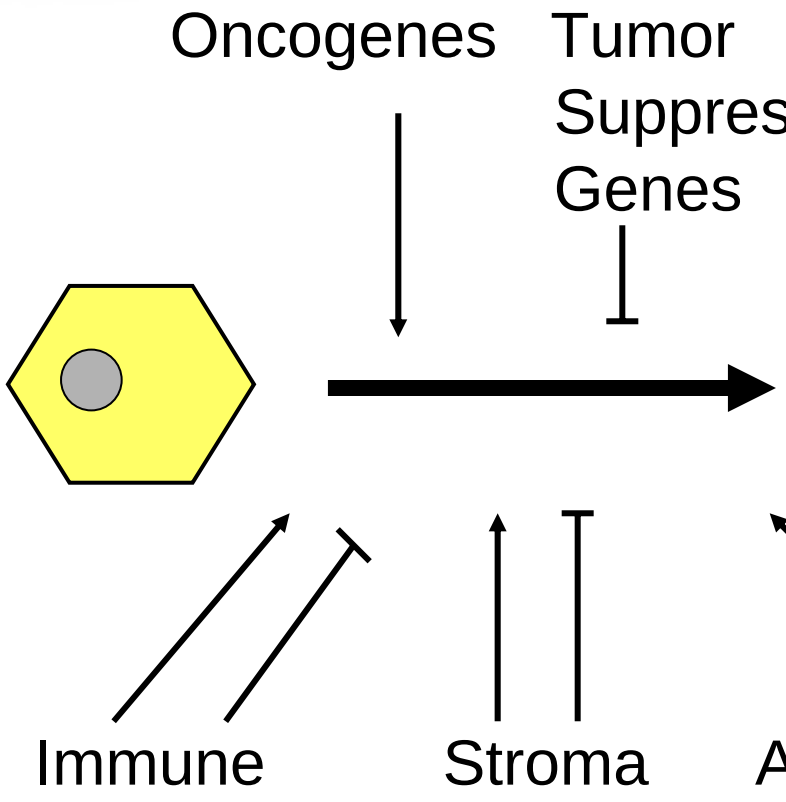
Image courtesy of *Nature*, Feb. 15, 2001

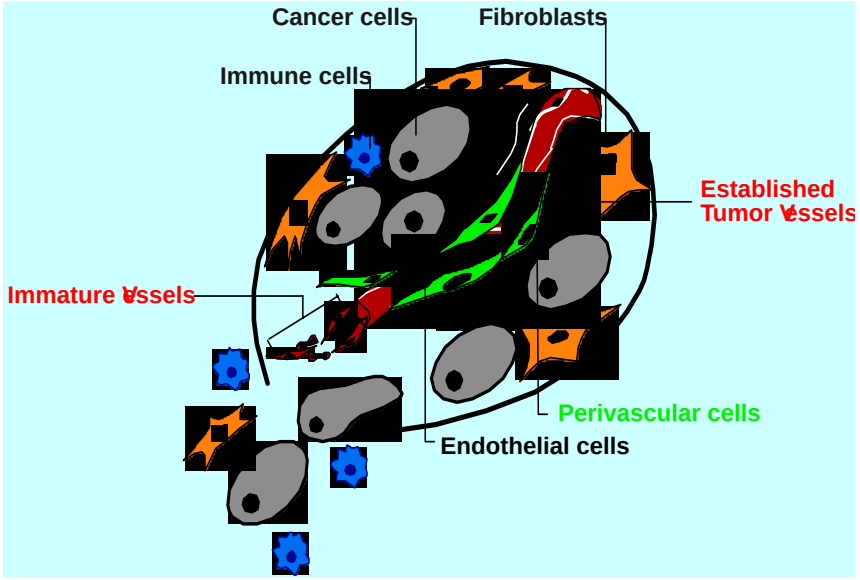
The Future – Molecular Medicine

Advances in Molecular Research and Technologies

The Past Century	21st Century
Established system to treat established disease – a treatment/therapeutic focus (in cancer often too late)	Gradual shift to targeted Interventions for prevention and treatment – shift in focus to early detection and prevention
Morphologic and pathologic diagnosis – drove treatment	Driven by the molecular characterization of disease – mechanistic understanding of pathways and processes
Expensive in all respects – not sustainable in 21st century	Evidence based – preserves human and financial capital – sustainable – Health becomes major national asset
Healthy population not a focus as a major national advantage/asset	

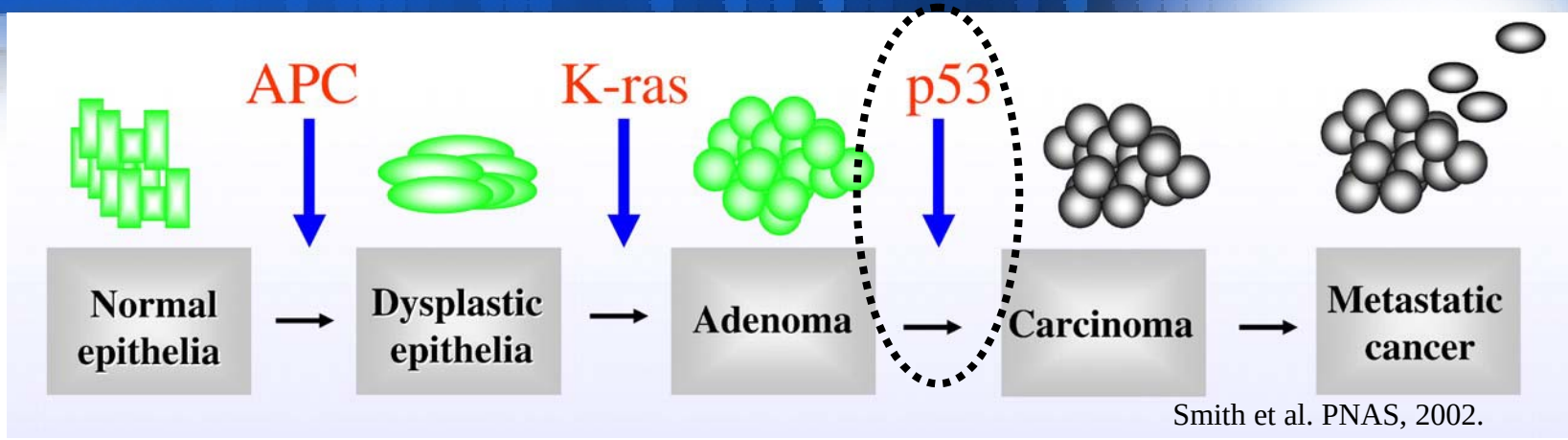
Why is it so Difficult? Cancer's Complexity





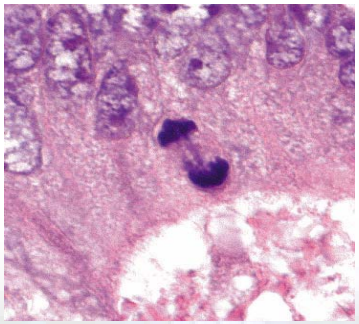
Courtesy Ron DePinho

The Carcinogenesis Process*: The Origin of Cancer's Complexity



Smith et al. PNAS, 2002.

Chr. Structural Aberrations	+/-	+++	+++
Telomerase activity	+/-	++	+++



*Colon Cancer

Lenhard Rudolph
Marcus Bosenberg
Slide – Ron Depinho

What Must We Achieve to Make Molecular Oncology a Reality

- A thorough understanding of genetic aberrations across the continuum of the carcinogenesis process (biomarkers)
- A correlative understanding of proteomic changes across this process (biomarkers)
- A mechanistic associated understanding of changes to signaling pathways
- A complete understanding of the natural history of every cancer – “mapped through biomarkers
- Targets – targets – targets
- Targeted diagnostics
- Targeted drugs and biologics for treatments and prevention

All of these major milestones have a common unifying need for the highest quality biospecimens – uniformly collected, annotated and managed and broadly available

The Promise of Biomarkers for Molecular Oncology

- New **target discovery** (understand underlying biology)
- Drug **development** – markers of toxicity, metabolism, etc.
- **Early detection** (broad or specific detection / corroboration of specific disease stage)
- Identify **molecular basis of disease phenotypes**
- Assessment of disease **aggressiveness**
- **Rational** choice of **treatments**
- **Assessment** of treatment **effectiveness**
- **Prevention markers**

Biomarker Discovery is Dependent on Harmonizing Biospecimens Across Laboratories/Sectors

Realizing the Promise of Molecular Oncology: NCI's Strategy to Accelerate Progress

- Redouble Support for Discovery and Innovation
- Deal with the Data Deluge - Connect the Enterprise - Bioinformatics
- Provide Common Research Infrastructure – Biospecimens, Genomics, Proteomics
- Apply, Provide, Leverage Advanced Technologies – Advanced Imaging, Nanotechnology
- Ensure Delivery Through Outcomes Research, Economic Models
- Reform Clinical Trials
- Build Science-/Based Partnerships with Regulatory Bodies

Enabling the Future to Realize the Potential of Molecular Oncology and Molecular Medicine

The National Cancer Institute:

- **Launched caBIG™ to provide IT infrastructure for "connectivity", biobanks, and large-scale database development and management and inter-institutional, multi-institutional and (cross-sector) studies**
- **Launched the NCI Alliance for Nanotechnology in Cancer to support and accelerate advanced systems that can interact with and interrogate cells for diagnosis and treatment**
- **Will soon launch a national proteomics-based program in biomarker discovery to provide common infrastructure**
- **Is collaboratively developing and will soon launch a pilot program to characterize the human cancer genome**

These and many other initiatives required to realize the future of personalized molecular medicine have a common need – human biospecimens.

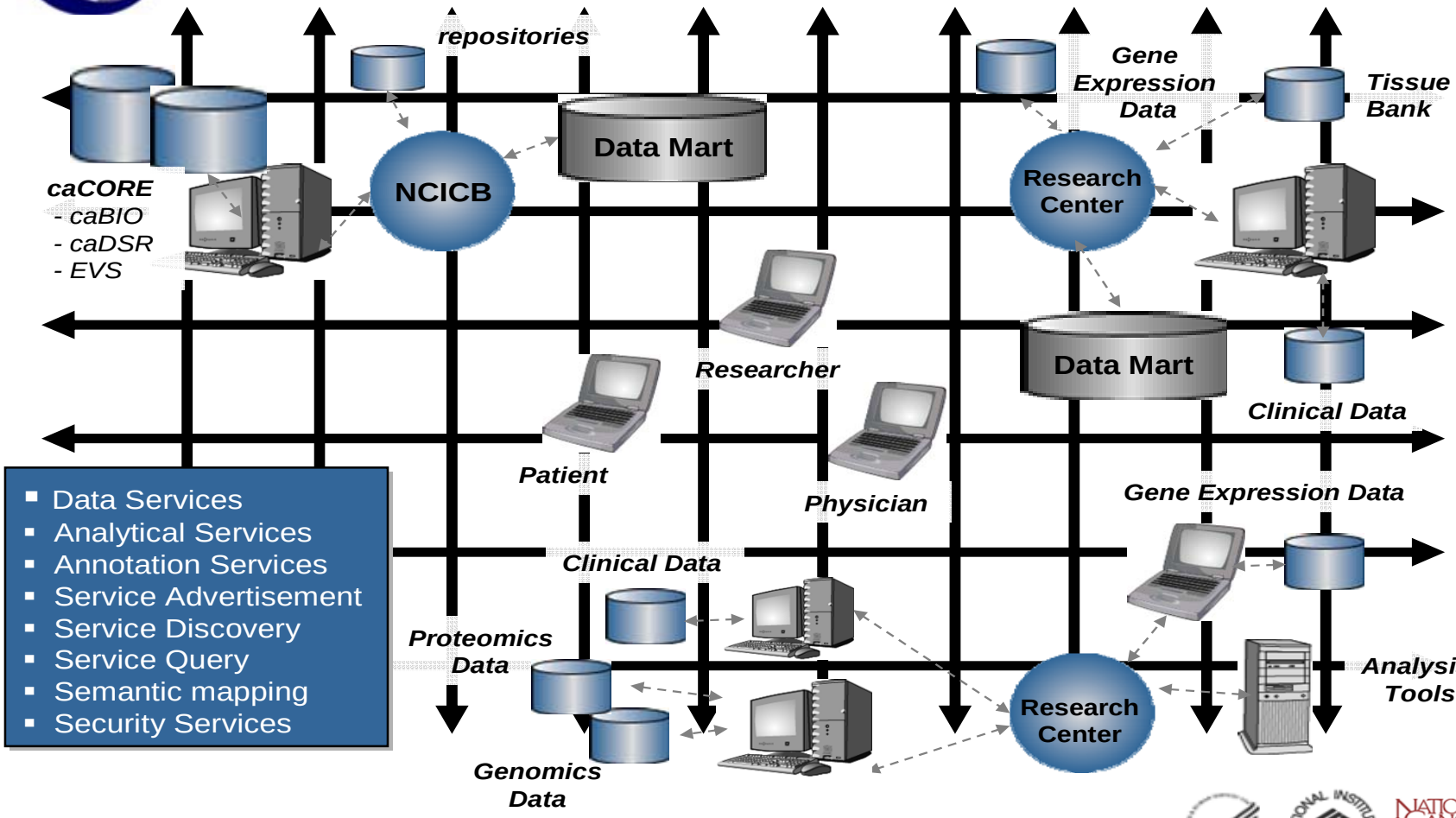
Networks, Advanced Technologies, Platforms

- **Basic Infrastructure**
  - **Bioinformatics – caBIG**
  - **Biospecimens – biobanks***
- **Common Technology Platforms**
  - Biomarkers - Proteomics*
  - Human Cancer Genome Pilot Project*
  - Clinical Research
- **Advanced Technologies**
  - Advanced Imaging
  - Nanotechnology*
- **Partnerships**

caBIG cancer Biomedical Informatics Grid

Center for Bioinformatics

caGrid



One Example: The NCI-NHGRI Human Cancer Genome Pilot Project

Goal: A three-year pilot to address key questions to determine the feasibility of a full-scale project that will ultimately facilitate the development of a complete "catalogue" of all genetic alterations in cancer

Enabling Factors:

- Significant knowledge base resulting from the NCI's investments in understanding molecular biology and genetics of many cancers
- Rate of progress of genomics analysis technologies - $1,000 genome sequencing looking possible
- NHGRI's complimentary high throughput projects

Key Emerging Issue for the HGCP: Samples, Samples, Samples

- Biospecimens identified as perhaps the major issue
- The ideal for this project:
  - source - clinical trial (simple vs. complex)
  - fresh frozen
  - matched normal and blood
  - sufficient quantity
  - single histopathologic type
  - single grade and single stage
  - low contamination

Some Musts for the Human Cancer Genome Project Biospecimens

- Prospective samples
- High level of pathologic QC
- Clear SOPs for all aspects of collection, etc.
- Quality assured processing and storage
- Fail safe bioinformatics system
- Uniform, complete annotation
- Systems monitoring – standards testing
- Possible use of retrospective collections – tough to pass muster

Proteomics requires higher level of quality in all aspects of biospecimen acquisition and management

Proteomics – Same Problems – but Worse – Real Problems for the Field *

(No technology currently interrogates more than 1% of the proteome)

A. Gel Based

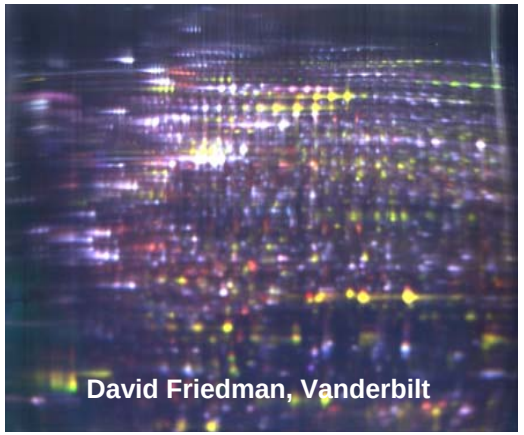
- 2-D Gel electrophoresis
- LC / LC / Gel electrophoresis

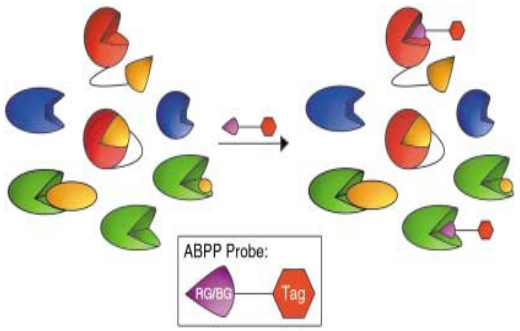
B. Mass Spectrometry Based

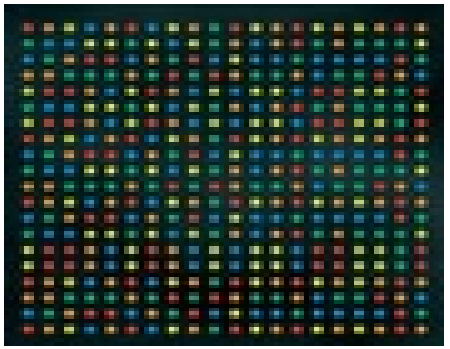
- LC proteins - MS / MS protease derived peptides
- LC / MS / MS - complex peptide mixtures
- MALDI MS – direct tissue analysis, activated surfaces

C. Chip / Array Based

- Antibody probes
- Activity based probes
- Chemically activated surfaces







* Slide from Richard Caprioli

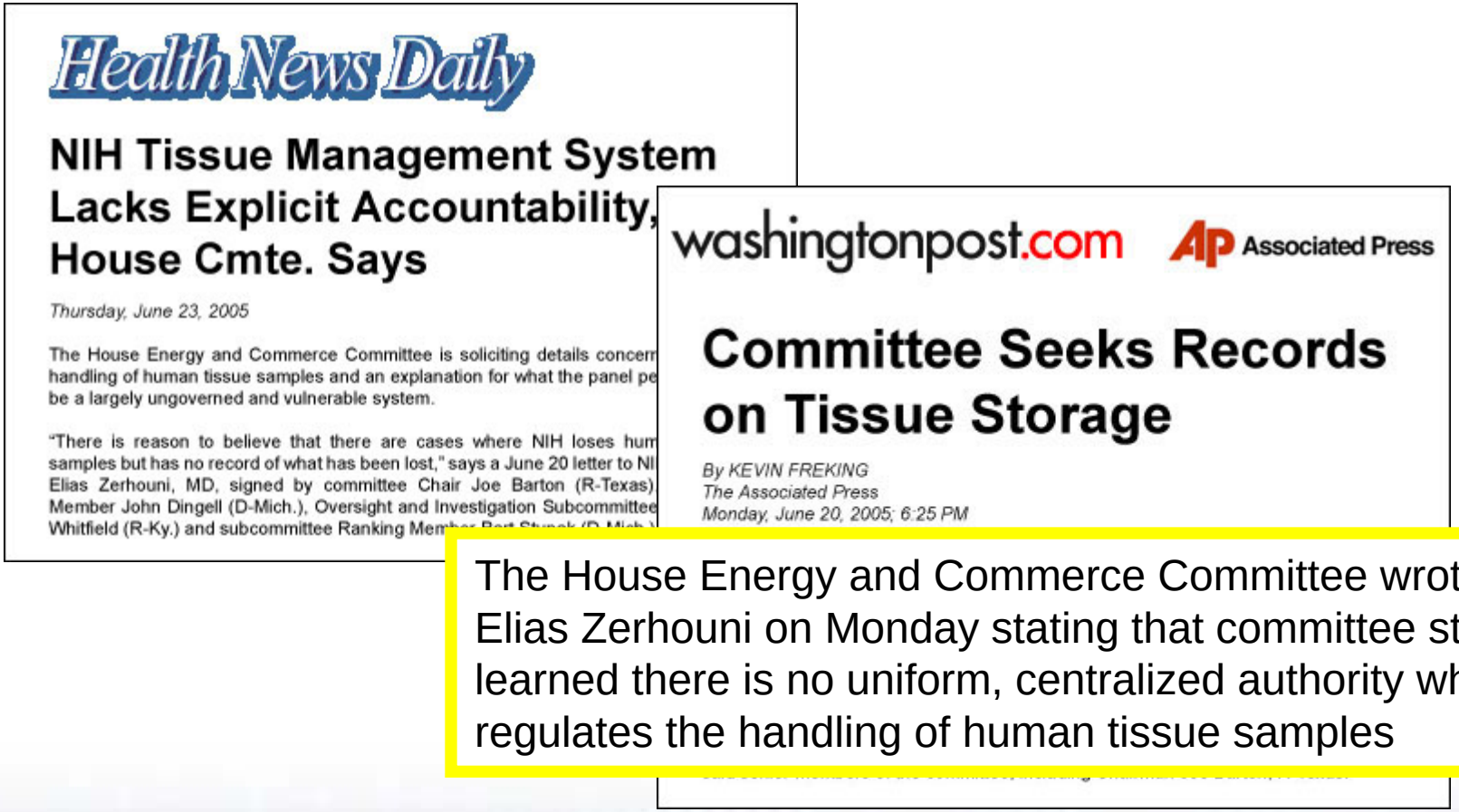
NCI Initiative to Address Problems in Proteomics

- Broad consortia to **standardize samples, proteomics technologies and develop protocols using common and specific models**
- Multidisciplinary teams
- Coordinated and virtually integrated
- Real time data exchange – broad access - reproducibility
- Large numbers of standardized antibodies
- Standards development
- High throughput capabilities
- Funds to drive proteomics technology development
- Common data capture, analysis, and interrogation platforms

A Few Challenges: The Overall State of NCI's Biobanks

- No unified system with broad access
- Much of tissue collection and/or storage practices not compatible with genomic/proteomic analysis
- Data comparison reproducibility difficult
- HIPAA and legal concerns as data is shared
- "Ownership" barriers - impede tissue sharing among researchers
- Role of pathology
- Data from tissues sold to companies are not in the public domain

Current Government-Supported Biorepositories May Not Fulfill the Public Trust



Health News Daily

NIH Tissue Management System Lacks Explicit Accountability, House Cmte. Says

Thursday, June 23, 2005

The House Energy and Commerce Committee is soliciting details concern handling of human tissue samples and an explanation for what the panel pe be a largely ungoverned and vulnerable system.

"There is reason to believe that there are cases where NIH loses hum samples but has no record of what has been lost," says a June 20 letter to NI Elias Zerhouni, MD, signed by committee Chair Joe Barton (R-Texas) Member John Dingell (D-Mich.), Oversight and Investigation Subcommittee Whitfield (R-Ky.) and subcommittee Ranking Mem

washingtonpost.com AP Associated Press

Committee Seeks Records on Tissue Storage

By KEVIN FREKING
The Associated Press
Monday, June 20, 2005; 6:25 PM

The House Energy and Commerce Committee wrote Dr. Elias Zerhouni on Monday stating that committee staff has learned there is no uniform, centralized authority which regulates the handling of human tissue samples

NCI's Tortuous Path: Solving the Biospecimen Biobanking Challenge

- **2002**
  - Biorepositories identified as area of critical importance - internal and external review process
  - Initial NCI surveys, community forums
- **2003**
  - Collaborated on RAND Report and NBN Blueprint published
  - Prostate pilot planning initiated
- **2004**
  - Study of NCI biorepositories
  - Prostate cancer pilot project developed
- **2005**
  - Biospecimen Coordinating Committee (BCC) and OBBR
  - Whitepapers finalized
  - Two unprecedented workshops
  - Reports to Boards
  - Guidelines development
  - Launch of Prostate Pilot Project

NCI Office of Biorepositories and Biospecimen Research (OBBR)

- NCI took steps to recognize the critical nature of biorepository resources – established the OBBR in 2005
- OBBR will work with its' Biospecimen Coordinating Committee to coordinate biorepositories and biorepository research across the NCI
- This office will be accountable for progressing from 1st generation guidelines to data-driven biorepository standards and practices

NCI Biorepository Coordinating Committee (BCC)

The NCI-Wide Biorepository Coordinating Committee Advises Leadership on Issues Related to the Harmonization of Procedures and Policies Related to NCI-Supported Biobanks

2005 Biospecimen Collection, Etc. Workshop

- Purpose and Use of Biorepositories
- Cross-Cutting Issues for Biorepositories
- Analytical Methods for Biospecimen-Based Research
- Best Practices for Biospecimen Collection, Processing, Storage, Retrieval, and Dissemination
- Establishing Biorepository Evaluation and Monitoring Criteria
- Access to Biospecimens
- Designing Repositories to Support Research with Emerging Technologies
- Priority Setting for Biorepositories

2005 Ethics, Legal and Policy (ELP) Workshop Topics

- Informed Consent
- Privacy, Confidentiality, and Data Security Protections
- IRBs and Governance
- Ownership, Legal, and Policy Issues
- Access to Biospecimens and Data

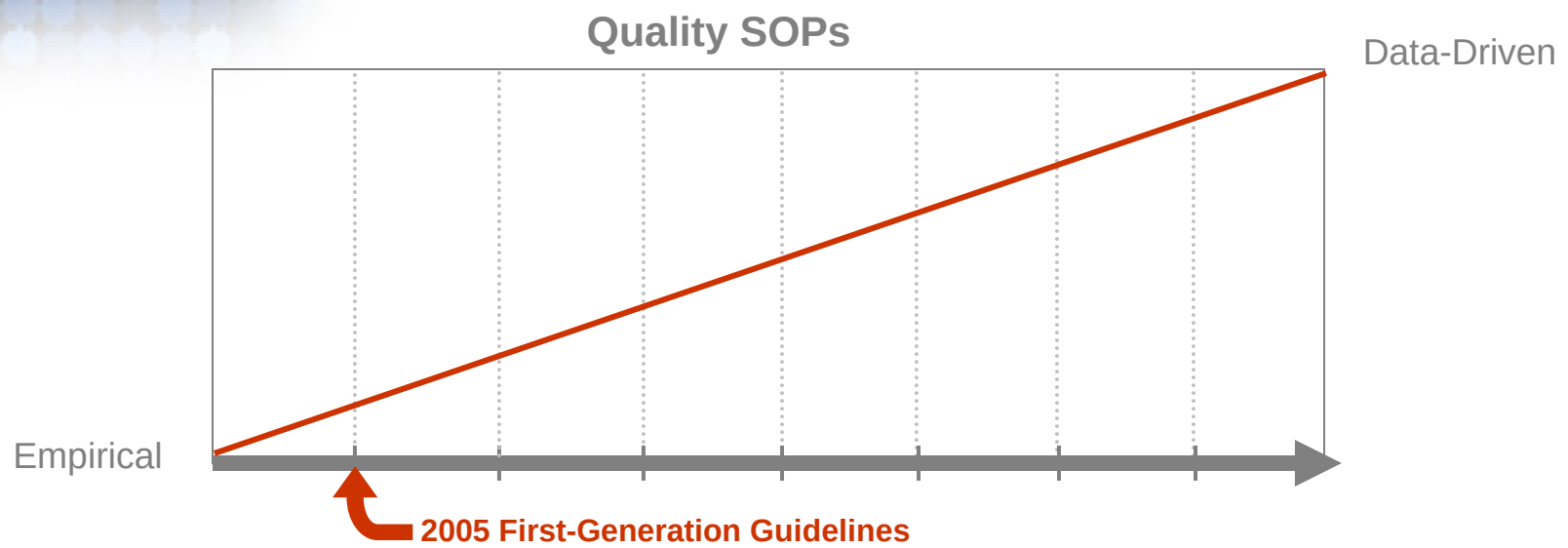
NCI Biobanks: Recommendation Categories

- Optimizing Biorepositories for Cancer Research
- Implementing Quality Assurance and Quality Control
- Implementing Informatics Systems
- Categorizing and Assessing Biorepositories
- Addressing Ethical, Legal, and Policy Issues
- Establishing Reporting Mechanisms
- Providing Administration and Management Structure

Culmination of Multi-Year "Due Diligence" Process

NCI is developing a long-term evidence-based solution –
Beginning with the promulgation of
Cancer Enterprise Best Practices/Standards for Biospecimens
– First-Generation Guidelines –
First Quarter 2006

NCI's Path from First-Generation Guidelines to Evidence-Based Biospecimens/Biobanks



Medical/ Surgical Procedures | Acquisition | Handling/ Processing | Storage | Distribution | QC/QA | Restocking Unused Sample

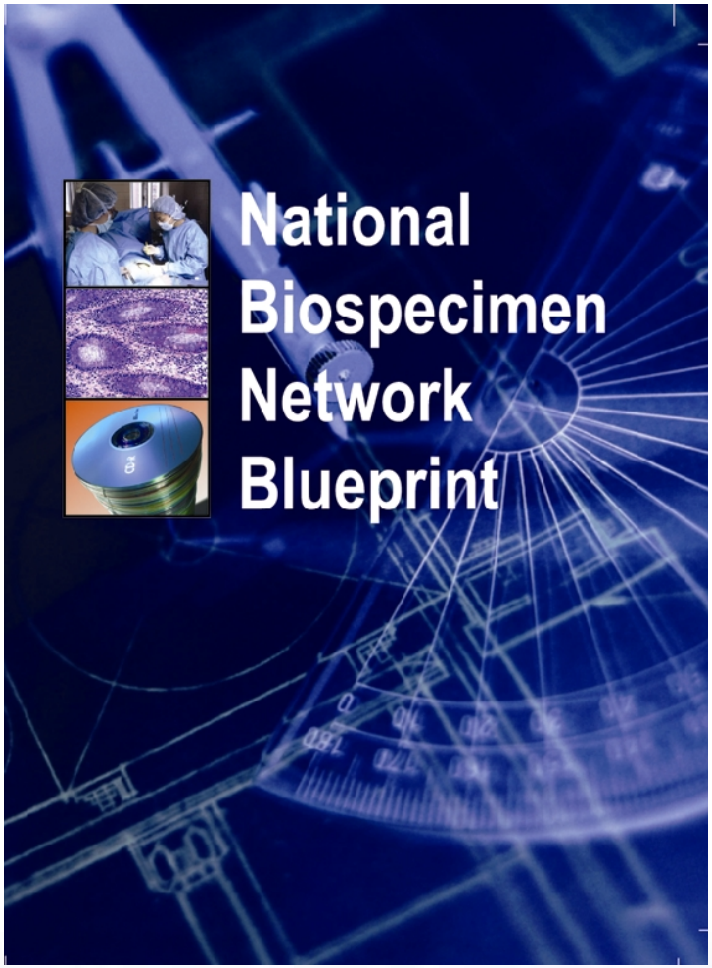
NCI's Future Strategy– Optimize Our Biobanks – Collaborate on Developing a National Resource – Harmonize Internationally

- **NCI Goals for 2006 and Beyond:**
  - **Large numbers of high-quality, clinically annotated samples**
  - **Diversity of cancer types and populations**
  - **Pathology and clinical (including longitudinal) annotation of specimens**
  - **Access through a centralized peer-review process**
  - **Management of ethical and legal issues for a chain of trust**
  - **Resources provided without intellectual property restrictions**
  - **Best practices-based SOPs for reproducible results**
  - **Bioinformatics infrastructure for building *in silico* capability**

One Way Forward to Enable Personalized Medicine

National Biospecimen Network Blueprint: "A Model for the Community – A Path for the Future of Personalized Medicine"

www.ndoc.org/about_ndc/reports/



Not Simple: Why is it Potentially More Difficult to Build a National Biorepository in the U.S.?

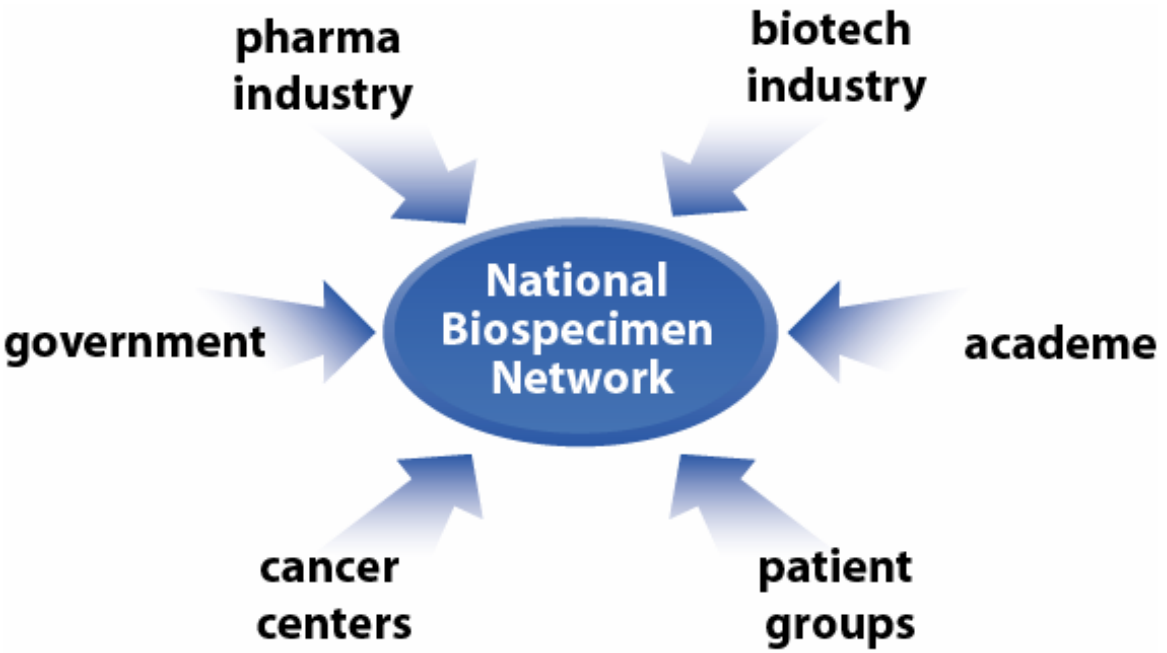
- **Lack of connectivity**
  - 300+million samples do not a “network” make…
  - Need a federated, coordinated approach for cancer...e.g., Cancer Centers or SPORES
- **Existing Biorepositories**
  - It’s difficult to re-fuel the airplane when it’s in the air.
  - We must determine what has value…sustain it…move on
- **Lack of Funding**
  - Source of funding and balance between sectors is unclear
  - Lack of reimbursement for biospecimens – pathologists
- **Evolution via Individual Initiated Grants - Control**

SPORE NBN Pilot Project Launch

- **Concept**
  - A study designed to pilot key aspects of an NBN-like concept
- **Goal**
  - Development of a common biospecimen coordination system and informatics infrastructure for collaborative SPORE projects in prostate cancer

What We Need to Build the National Biospecimen Network?

- Commitment to the concept of a national, standards-driven biorepository network
- Leadership in converting the concept to a reality
- Participation by all sectors in implementing such a new system
- International Integration
- Funding



The Promise of Highest-Quality Biobanks for Molecular Oncology and Personalized Medicine

- A comprehensive national system to manage biospecimen and clinical data collection and dissemination
- Broad comparability of research results — SOPs based in evidence-based best practices
- Statistically powerful datasets to empower genomics/proteomics research
- Support for high-throughput research — e.g., identification and validation of biomarkers
- Over time — in silico research through continually expanding database
- International harmonization possible

Enable major advances in targeted diagnosis, prevention, treatment, and clinical outcomes for cancer – and all diseases

National Cancer Act of 1971

Our Hope for Personalized Medicine: Molecular Oncology in a Decade

President Richard Nixon signs
National Cancer Act on December 23, 1971

“Make the Conquest of Cancer a National Crusade”

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